

### REMARKS

In response to the Office Action mailed March 24, 2004, Applicants renumbered originally numbered claims 30-45 as claims 29-44, respectively. Throughout the remarks below, Applicants refer to the numbering of the claims in accordance with the claims as renumbered. In addition, Applicants amended claims 10-16, 18, 20-24, 26-29 and 33-37, cancelled claims 1-9, 17, 19, 25, 30-32 and 38-44, and added new claims 45-66. Claims 10-16, 18, 20-24, 26-29, 33-37 and 45-66 are presented for examination.

#### 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 10-16, 18-24, 26-29, and 31-37, under 35 U.S.C. §112, first paragraph as purportedly failing to satisfy the enablement requirement.<sup>1</sup> In *In re Wands* 858 F.3d 731 (Fed. Cir. 1998), the United States Court of Appeals for the Federal Circuit described the factors to be considered and balanced when determining whether a disclosure satisfies the enablement requirement. Each of these factors is discussed below with respect to the claims.

##### The nature of the invention:

The invention generally relates to the use of a three-dimensional structure of a polypeptide including at least a core region of a free RGS4 protein. The uses include selecting a potential modulator of an RGS protein (claim 10 and its dependent claims), determining the interaction between a candidate species and a free RGS protein (claim 18 and its dependent claims), designing a potential modulator that will form a bond with one or more amino acids in a binding site of an RGS4 protein and determining whether the potential modulator inhibits or promotes the activity of RGS or RGS4/G $\alpha$  complex (claim 20 and its dependent claims, claim 23 and its dependent claims, claim 26 and its dependent claims) and selecting a potential antagonist or agonist of an RGS protein.

##### The level of one of ordinary skill in the art:

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<sup>1</sup> Claims 19, 31 and 32 were cancelled, so the rejection of these claims should be withdrawn.

In general, one of ordinary skill in the art would likely have a B.S. or a Ph.D. in biology (e.g., protein biology).

The state of the prior art:

No one has previously disclosed or suggested the methods covered by the pending claims.

The breadth of the claims:

The subject matter covered by the claims is no broader than Applicants' contribution.

The level of predictability in the art:

The relevant art is generally unpredictable. However, as discussed below, the present application discloses sufficient information to allow one of ordinary skill in the art to successfully implement the methods covered by the claims.

The existence of working examples:

Applicants disclose a working example that describes the determination of the three-dimensional structure of the core region of RGS4, as well as the identification of an allosteric binding site in the core region of RGS4. (See, e.g., Application at page 28, line 19-page 36, line 2 and Figs 1 and 2B.) Applicants disclose specific working examples that describe assays that test for modulators of RGS4 binding to  $G_{\alpha i1}$  and modulators of RGS4 GTPase activity. (See, e.g., id. at page 33, line 23-page 36, line 2.)

The amount of direction provided by the inventor:

The application provides sufficient direction to one of ordinary skill in the art. As noted above, Applicants disclose the three-dimensional structure of the core region of RGS4. (See, e.g., id. at page 28, line 19-page 33, line 21) Applicants also disclose methods of identifying and assaying compounds that can modify the activity of the core region of RGS4 protein. (See, e.g., id. at page 36, lines 3-24.) Applicants further disclose specific examples that describe assays that test for modulators of RGS4 binding to  $G_{\alpha i1}$  and modulators of RGS4 GTPase activity. (See, e.g., id. at page 33, line 23-page 36, line 2.) In addition, Applicants also disclose homology modeling and molecular replacement techniques. (See, e.g., id. at page 19, line 10-page 21, line 29.) Using these techniques, one skilled in the art can use the three-dimensional structure of the

core region of RGS4 to determine the three-dimensional structure of other RGS proteins. (See, e.g., id.)

The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. (See M.P.E.P §2164.01 citing *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom.*) As explained above, Applicants have not only disclosed working examples, but have also disclosed specific modeling and analysis techniques (e.g., homology modeling and molecular replacement). Accordingly, the quantity of experimentation needed to make and use the invention is not undue.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph.

35 U.S.C. §112, Second Paragraph

Claims 10-16, 18, 19-24, 26-28, 29, and 31-37 were rejected under 35 U.S.C. §112, second paragraph as being indefinite on a number of bases.<sup>2</sup>

The Examiner stated that the phrases "portion thereof" (claim 10), "reversible or nonreversible bond" (claims 20, 23, 26), and "capable of binding to" (claims 34-37) rendered these claims indefinite. Without conceding that these bases of the rejection are appropriate, Applicants amended the claims to remove these phrases.

The Examiner also stated that the phrases "interaction", "predicted by its interaction" and "interact" rendered claims 10-12, 14, 18, 19, 21, and 24 indefinite. But, these terms would be readily understood by one skilled in the art. Indeed, the term "interact" is defined as "to act upon one another", and the term "interaction" is defined as "mutual or reciprocal action or influence". (See, e.g., Merriam-Webster's Collegiate Dictionary, 10<sup>th</sup> Edition, Merriam-Webster,

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<sup>2</sup> Claims 19, 31 and 32 were cancelled, so the rejection of these claims should be withdrawn.

Incorporated, Springfield, MA, 1997 at 609 (copy enclosed)). These definitions are consistent with the manner in which the terms are used in the specification and claims.

The Examiner rejected claims 28, 29, and 31-37 for missing essential steps and or for lacking proper antecedent basis. Applicants amended and/or cancelled these claims to obviate these bases of the rejection.

In view of the foregoing, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. §112, second paragraph.

35 U.S.C. §102(a)

The Examiner rejected claims 10-16, 18-24, 26-29, and 31-37 under 35 U.S.C. §102(a) as being anticipated by Alba *et al.* ("Alba").<sup>3</sup> However, Alba does not disclose a three-dimensional structure of a polypeptide including at least a core region of a free RGS4 protein, as required by the pending claims. Instead, Alba discloses the three-dimensional structure of a complexed RGS4 protein (which is not a free RGS4 protein) and the three-dimensional structure of GAIP (which is not an RGS4 protein). (See Alba at Abstract). Accordingly, Applicants request reconsideration and withdrawal of the rejection under 35 U.S.C. §102(a).

35 U.S.C. §103(a)

The Examiner rejected claims 10-16, 18-24, 26-29, and 31-37 under 35 U.S.C. §103(a) for being obvious in light of Koradi *et al.* (Koradi).<sup>4</sup> In making this rejection, the Examiner indicated that certain limitations were directed to "non-functional descriptive material". Without conceding that the Examiner's statement is correct, the Examiner seems to have completely ignored claim limitations that are clearly not directed to "non-functional descriptive material." Specifically, the Examiner ignored at least the following limitations "selecting a potential modulator" (claim 10 and its dependent claims), "determining the interaction between a candidate species" (claim 18 and its dependent claims), "designing a potential modulator" (claim 20 and its dependent claims, claim 23 and its dependent claims, claim 26 and its dependent

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<sup>3</sup> Claims 19, 31 and 32 were cancelled, so the rejection of these claims should be withdrawn.

<sup>4</sup> Claims 19, 31 and 32 were cancelled, so the rejection of these claims should be withdrawn.

claims), "select[ing] a potential agonist or antagonist" (claim 28 and its dependent claims. Koradi does not disclose, or even suggest, any of these limitations. Applicants therefore request reconsideration and withdrawal of the rejection under 35 U.S.C. §103(a).

#### Claim Objections

The Examiner objected to claims 10-14, 16, 18-21, 23, 24, 26, 28, 29, and 31-37 because of the use of the abbreviation "RGS" in these claims.<sup>5</sup> As noted by the Examiner, however, this term is explained in the specification, and Applicants see no reason why the term may not be properly used in the claims.

The Examiner objected to claim 27 because of a typographical error. Applicants corrected this error to obviate this rejection.

In view of the foregoing, Applicants request reconsideration and withdrawal of the objections to the claims.

#### Conclusion

Applicants believe the application is in condition for allowance, which action is requested.

No fees are believed to be due. However, any necessary charges or credits can be applied to Deposit Account No. 06-1050, with reference to Attorney Docket No. 16163-021002.

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<sup>5</sup> Claims 19, 31 and 32 were cancelled, so the objection of these claims should be withdrawn.

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Respectfully submitted,

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